What is claimed is:

1. A polypeptide comprising the amino acid sequence of SEQ ID NO: 4; wherein at least one of the seven variable positions of SEQ ID NO: 4 has an amino acid residue that differs from that of the corresponding wild-type Hdm2(17-125) amino acid sequence (SEQ ID NO: 2); and wherein said polypeptide optionally comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11 conservative amino acid substitutions that are not at one of the seven variable positions of SEQ ID NO: 4.

2. The polypeptide according to claim 1, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 and SEQ ID NO: 12; wherein any one of said amino acid sequences optionally comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11 of said conservative amino acid substitutions.

3. The polypeptide according to claim 2, wherein said polypeptide optionally comprises 1, 2, or 3 of said conservative amino acid substitutions.

4. The polypeptide according to claim 3, wherein said polypeptide comprises the amino acid sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 and SEQ ID NO: 12.

5. The polypeptide according to claim 4, wherein said polypeptide consists of the amino acid sequence of selected from the group consisting of SEQ ID NO: 6 and SEQ ID NO: 10.

6. A nucleic acid encoding the polypeptide according to claim 1.

7. The nucleic acid according to claim 6 comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, and SEQ ID NO: 11.

8. An expression vector comprising the nucleic acid according to claim 7, wherein said expression vector further comprises a transcriptional control sequence operatively linked to the nucleic acid.

9. A host cell comprising the expression vector according to claim 8.

10. A method for producing a modified Hdm2 protein, comprising culturing the host cell according to claim 9 in a culture medium under conditions in which the nucleic acid encoding the modified Hdm2 protein is expressed.

11. The method according to claim 10 wherein the host cell is an E coli cell.

12. A method of obtaining a purified modified Hdm2 protein, comprising purifying the modified Hdm2 protein produced by the method according to claim 10 from the culture medium.

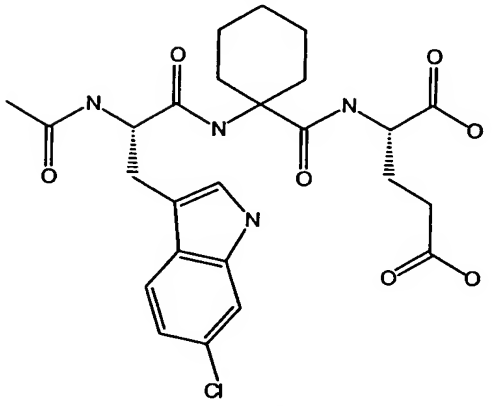
13. A method for identifying an agent for use as an inhibitor of Hdm2 comprising:

(a) contacting the potential agent with the polypeptide according to claim 1 and a p53 substrate; and

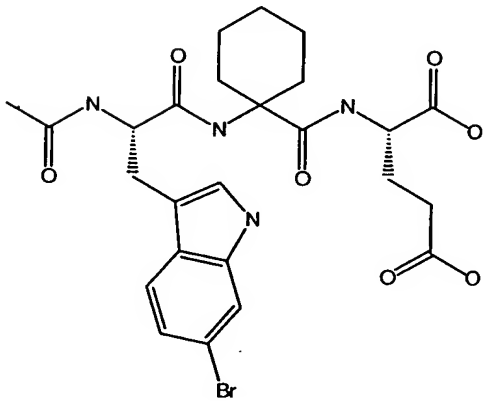
(b) determining the ability of the polypeptide to bind to the p53 substrate;

wherein a potential agent is identified as an agent that inhibits Hdm2 when there is a decrease in the binding of the polypeptide and the p53 substrate in the presence of the agent relative to in its absence.

14. A compound selected from the group consisting of



and



15. A polypeptide-compound complex comprising the compound according to claim 14 and a polypeptide complexed to it, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 4, wherein at least one of the seven variable positions of SEQ ID NO: 4 has an amino acid residue that differs from that of the corresponding wild-type Hdm2(17-125) amino acid sequence (SEQ ID NO: 2); and wherein said polypeptide optionally comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11 conservative amino acid substitutions that are not at one of the seven variable positions of SEQ ID NO: 4.

16. A crystal comprising a polypeptide, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 4, wherein at least one of the seven variable positions of SEQ ID NO: 4 has an amino acid residue that differs from that of the corresponding wild-type Hdm2(17-125) amino acid sequence (SEQ ID NO: 2); and wherein said polypeptide optionally comprises 1,

2, 3, 4, 5, 6, 7, 8, 9, 10 or 11 conservative amino acid substitutions that are not at one of the seven variable positions of SEQ ID NO: 4.

17. The crystal according to claim 16, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 and SEQ ID NO: 12; wherein any one of said amino acid sequences optionally comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11 of said conservative amino acid substitutions.

18. The crystal according to claim 17, wherein said polypeptide optionally comprises 1, 2, or 3 of said conservative amino acid substitutions.

19. The crystal according to claim 18, wherein said polypeptide comprises the amino acid sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 and SEQ ID NO: 12.

20. The crystal according to claim 19, wherein said polypeptide consists essentially of the amino acid sequence of selected from the group consisting of SEQ ID NO: 6 and SEQ ID NO: 10.

21. The crystal according to either of claims 16 or 20, wherein said crystal effectively diffracts X-rays to a resolution of greater than 5.0 Å.

22. The crystal according to claim 21, wherein said crystal effectively diffracts X-rays to a resolution of greater than 2.5 Å.

23. The crystal according to claim 22, wherein said crystal effectively diffracts X-rays to a resolution of greater than 1.5 Å.

24. The crystal according to either of claims 16 or 20, wherein said polypeptide is complexed to a compound that binds said polypeptide and forms a polypeptide-compound complex.

25. The crystal according to claim 24, wherein said compound is selected from the group consisting of a peptide derived from p53, SCH549128, Ac-^{6Cl}WAC$_{3c}$E and Ac-^{6Br}WAC$_{3c}$E .

26. The crystal according to claim 16, wherein said polypeptide consists of the amino acid of SEQ ID NO: 10 and said crystal has the structural coordinates as set forth in Table 3.

27. The crystal according to claim 16, wherein said polypeptide consists of the amino acid of SEQ ID NO: 6 and said crystal has the structural coordinates as set forth in Table 4.

28. A crystal comprising a polypeptide, wherein said polypeptide is characterized by structure coordinates comprising a root mean square deviation (RMSD) of conserved residue backbone atoms of less than about 2.0 Å when superimposed on backbone atoms described by structural coordinates of Table 3 or Table 4.

29. The crystal according to claim 28, wherein said RMSD is less than about 1.5 Å.

30. The crystal according to claim 29, wherein said RMSD is less than about 1.0 Å.

31. The crystal according to claim 30, wherein said RMSD is less than about 0.5 Å.

32. The crystal according to claim 28, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 4, wherein at least one of the seven variable positions of SEQ ID NO: 4 has an amino acid residue that differs from that of the corresponding wild-type Hdm2(17-125) amino acid sequence (SEQ ID NO: 2); and wherein said polypeptide optionally comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11 conservative amino acid substitutions that are not at one of the seven variable positions of SEQ ID NO: 4.

33. The crystal according to claim 32, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 8 or SEQ ID NO: 12.

34. A method for producing a crystal comprising the polypeptide according to claim 1, comprising

a) providing said polypeptide; and

b) incubating said polypeptide under conditions in which a crystal of said polypeptide is formed.

35. The method according to claim 34, wherein

said providing comprises providing a solution comprising said polypeptide; and said incubating comprises

(i) mixing said solution with a precipitant to produce a polypeptide-precipitant mixture; and

(ii) incubating said mixture in a sealed container in close proximity to a reservoir of said precipitant under conditions in which a crystal of said polypeptide is formed.

36. The method according to claim 35, wherein said polypeptide comprises the amino acid sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 and SEQ ID NO: 12.

37. The method according to claim 36, wherein said polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NO: 6 and SEQ ID NO: 10.

38. The method according to claim 35, wherein said mixing further comprises mixing a compound that binds said polypeptide with said polypeptide and said mixing forms a polypeptide-compound complex.

39. The method according to claim 38, wherein said compound is selected from the group consisting of a peptide derived from p53, SCH549128, Ac-^{6Cl}WAC$_{3c}$E and Ac-^{6Br}WAC$_{3c}$E.

40. A computer for producing a three-dimensional representation of the polypeptide according to claim 1 or a polypeptide-compound complex that comprises said polypeptide complexed with a compound that binds said polypeptide, wherein said polypeptide or said polypeptide-compound complex has a root mean square deviation from the backbone atoms of Table 3 or 4 of less than about 2.0 Å, wherein said computer comprises:

(a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises the structure coordinates of Table 3 or 4;

(b) a working memory for storing instructions for processing said machine-readable data;

(c) a central-processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine readable data into said three-dimensional representation; and

(d) a display unit coupled to said central-processing unit for displaying said three-dimensional representation.

41. The computer according to claim 40, wherein the root mean square deviation between the homologue and the structure coordinates set forth in Table 3 or 4 is less than about 1.5 Å.

42. The computer according to claim 41, wherein the root mean square deviation between the homologue and the structure coordinates set forth in Table 3 or 4 is less than about 1.0 Å.

43. The computer according to claim 42, wherein the root mean square deviation between the homologue and the structure coordinates set forth in Table 3 or 4 is less than about 0.5 Å.

44. The computer according to claim 40, wherein said polypeptide comprises the amino acid sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 and SEQ ID NO: 12.

45. The computer according to claim 44, wherein said polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NO: 6 and SEQ ID NO: 10.

46. The computer according to claim 40, wherein said polypeptide compound complex comprises a compound selected from the group consisting of a peptide derived from p53, SCH549128, Ac-^{6Cl}WAC$_{3c}$E and Ac-^{6Br}WAC$_{3c}$E.

47. The computer according to claim 40, wherein the display unit is displaying the three dimensional representation.

48. A method for obtaining structural information concerning a molecule of unknown structure, comprising generating X-ray diffraction data from a crystallized form of the molecule, and applying crystallographic phases derived from at least a portion of structure coordinates set forth in Table 3 or 4 to said X-ray diffraction pattern to generate a three-dimensional electron density map of at least a portion of the molecule.

49. A method for designing, selecting and/or optimizing a potential inhibitor of the polypeptide according to claim 1, comprising

(a) providing the structure coordinates of said polypeptide or of a polypeptide-compound complex comprising said polypeptide complexed to a compound on a computer comprising the means for generating three-dimensional structural information from said structural coordinates; and

(b) designing, selecting and/or optimizing said potential inhibitor by performing a fitting operation between said potential inhibitor and said three-dimensional structural information of said polypeptide or said polypeptide-compound complex.

50. The method according to claim 49, wherein said structure coordinates are set forth in Table 3 or 4 or comprise a root mean square deviation (RMSD) of conserved residue backbone atoms of less than about 1.5 Å when superimposed on backbone atoms described by structural coordinates of Table 3 or Table 4.

51. The method according to claim 50, wherein said RMSD is less than about 1.0 Å.

52. The crystal according to claim 51, wherein said RMSD is less than about 0.5 Å.

53. The crystal according to claim 52, wherein said RMSD is less than about 0.1 Å.

54. The method according to claim 50, further comprising after step (b),

(c) providing or synthesizing said potential inhibitor;

(d) contacting said potential inhibitor with said polypeptide; and

(e) determining whether the potential inhibitor binds to said polypeptide and inhibits its activity.

55. A method for evaluating the ability of a potential inhibitor to associate with the polypeptide according to claim 1 or of a polypeptide-compound complex comprising said polypeptide complexed to a compound, comprising

(a) employing computational means to perform a fitting operation between the structure coordinates of the potential inhibitor and the structure coordinates of the polypeptide or polypeptide-compound complex; and

(b) analyzing the results of said fitting operation to quantitate the association between the potential inhibitor and the polypeptide or polypeptide-compound complex.

56. The method according to claim 55, further comprising generating a three-dimensional graphical representation of the polypeptide or polypeptide-compound complex prior to (a).

57. The method according to claim 55, wherein said structure coordinates are set forth in Table 3 or 4 or comprise a root mean square deviation (RMSD) of conserved residue backbone atoms of less than about 2.0 Å when superimposed on backbone atoms described by structural coordinates of Table 3 or Table 4.